Department of Vermont Health Access
Pharmacy Benefit Management Program
DUR Board Meeting Minutes
May 17, 2016

Board Members:

Present:

Zail Berry, MD
Janet Farina, RPh
Clayton English, PharmD
Louise Rosales, NP
James Marmar, RPh
Patrica King, MD

Absent:

Staff:

Jacquelyn Hedlund, MD
GHS/Change HealthCare
Mike Ouellette, RPh, GHS/Change HealthCare
Scott Strenio, MD, DVHA
Mary Beth Bizzari, RPh, DVHA
Jennifer Egelhof, DVHA
Stacey Baker, DVHA
Nancy Hogue, Pharm D, DVHA
Thomas Simpatico, MD, DVHA
Jason Pope, DVHA
Laurie Pedlar, RPh, GHS/Change HealthCare
Jeffrey Barkin, MD, GHS/Change HealthCare

Guests:

Thomas Algozzine, Novartis
Kristen Bruno-Doherty, Astrazeneca
Megan Dotterer, GSK
Dave Downey, Abbott Labs
Susan Donnelly, Pfizer
Rodney Francisco, Sunovion
Franco Casagrande, Abbvie
Darren Keegan, Allergan
Hannah Parker, AstraZeneca
Kevin Kobylinski, Astellas
Lance Nicholls, Pfizer
Jessica Kritman, Abbott
George Small, AstraZeneca

1. Executive Session:

- An executive session was held from 6:00 p.m. until 6:30 p.m.

2. Introductions and Approval of DUR Board Minutes:

- Introductions were made around the table.
- The April meeting minutes were accepted as printed.

3. DVHA Pharmacy Administration Updates: Nancy Hogue, PharmD, DVHA

- As a result of the CMS covered outpatient drug rule, there will be upcoming changes to the pricing methodology for claims across all Medicaid. Vermont will soon pay on the actual acquisition cost plus a professional dispensing fee. Dispensing fee surveys will be required to get an idea of what the true cost of dispensing is. DVHA is in the development stages of this survey.
- DVHA is continuing to work on recruiting new members for the DUR Board.

4. Medical Director Update: Scott Strenio, MD, DVHA

- Dr. Strenio spoke with Dr. Chen, and he feels that a quantity limit for Narcan NS of 4 inhalers per month is sufficient.
    - Dr. Strenio will follow up on what the protocol is for receiving it through the health department.
- Follow up on the RetroDUR Asthma initiative: A letter was drafted by GHS and reviewed by Rhonda Williams at the VT Department of Health. It will tie in with the notice they send out in the fall. GHS and DVHA will be moving forward with getting the educational letters sent to providers.
- Follow up on the RetroDUR Multiple Benzo initiative: Scott continues to explore the possibilities and challenges of offering CBT to members with insomnia and multiple benzos. There will be more on this topic to come.

5. Follow-up Items from Previous Meetings:

- **Quantity Limits for Narcan® (Naloxone HCl) Nasal Spray**
    - GHS presented the updated criteria sheet with a quantity limit of 4 single use sprays/28 days.

Recommendation: Add quantity limit for Narcan® Nasal Spray 4 single use sprays/28 days.

Board Decision: The Board unanimously approved the above recommendation.

6. RetroDUR/DUR: GHS/Change Healthcare Jacqueline Hedlund,MD

a) **Introduce:** ***Diabetes/HTN-Appropriate Use of Angiotensin Modulators***

Hypertension is a common and serious problem in patients with both type I and type II diabetes. The incidence of hypertension rises from 5 % at 10 years, to 33% at 20 years and 70% at 40 years. The blood pressure usually rises within a few years after the onset of moderately increased albuminuria (microalbuminuria) and increases progressively as the renal disease worsens. Early treatment of hypertension is particularly important in the diabetic patient to prevent cardiovascular disease and slow progression of renal disease and diabetic retinopathy. The American Diabetes Association guidelines state that pharmacologic therapy for patients with diabetes and hypertension should comprise a regimen that includes either an ACE inhibitor or ARB, but not both, and that multiple drug therapy (including an ACE-I or ARB at maximal doses plus a thiazide diuretic) is generally required to meet blood pressure targets. Additionally, the target blood pressure is systolic blood pressure <140 mm Hg, and the diastolic target is < 90 mm Hg.

Recommendation: In order to evaluate provider compliance with guidelines and possible gaps in care, we will identify members with Diabetes, both type I and type II, who are hypertensive and quantify the use of ACE-I and ARB medications, either alone, or combined with other antihypertensive medications, including thiazide diuretics. The data source will be paid, non-reversed Medicaid pharmacy claims during calendar years 2014-2015, excluding members with Part D, VMAP, and Healthy Vermonters coverage.

Board Decision: None needed at this time.

7. Clinical Update: Drug Reviews: Dr. Jeffery Barkin GHS/Change Healthcare and Mike Ouellette, RPh GHS/Change Healthcare

Abbreviated New Drug Reviews:

- None at this time.

Full New Drug Reviews:

a) **Durlaza® Cap(asprin)**
   - Aspirin, the active ingredient of Durlaza®, is a platelet aggregation inhibitor. Aspirin, known as acetylsalicylic acid, inhibits prostaglandin synthesis, which results in inhibition of platelet aggregation for their lifespan (about 7-10 days). The dosage form is capsules, extended-release: 162.5mg taken once daily**.** The prescribing information indicated that when studied, the pharmacodynamic effect of Durlaza® is similar to that achieved with immediate-release aspirin dosed at 81mg. Aspirin has been shown to cause a statistically significant reduction in cardiovascular events in patients with previous cardiovascular disease (CVD) events.

Recommendation: The recommendation is for Durlaza ® to be non-preferred.

Clinical Criteria:

- Durlaza: The patient is ≥ 18 years of age AND the indication for use is to reduce the risk of death and myocardial infarction (MI) in patients with chronic coronary artery disease (history of MI, unstable angina pectoris, or chronic stable angina) OR to reduce the risk of death and recurrent stroke in patients who have had an ischemic stroke or transient ischemic attack AND the patient is unable to use at least 4 preferred products, one of which must be aspirin.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation with amended clinical criteria to require a trial of an enteric coated aspirin.

b) Nucala® INJ (mepolizumab)

- Mepolizumab, the active ingredient of Nucala®, is a humanized interleukin-5 (IL-5) antagonist monoclonal antibody that is produced by recombinant DNA technology in Chinese hamster ovary cells. IL-5 is the main cytokine for the growth and differentiation, recruitment, activation, and survival of eosinophils. Mepolizumab binds to IL-5, inhibiting the bioactivity of IL-5 and thus reducing the production and survival of eosinophils. Nevertheless, the exact mechanism of mepolizumab in asthma has not been conclusively established. It is indicated for the add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype. Nucala® is not indicated for treatment of other eosinophilic conditions or for the relief of acute bronchospasm or status asthmaticus. The recommended dose is 100mg given subcutaneously into the upper arm, thigh, or abdomen every 4 weeks. Nucala® should be reconstituted and administered by a healthcare professional. It is recommended to monitor patients after administration. The safety and efficacy of Nucala® were assessed in 3 double-blind, randomized, placebo-controlled trials, with one being a dose-ranging and exacerbation study (Trial 1) and two being confirmatory studies (Trials 2 and 3). The primary endpoint in Trials 1 and 2 was the frequency of exacerbations, defined as worsening of asthma requiring the use of oral/systemic corticosteroids and/or hospitalization and/or emergency department visits. Compared with placebo, the Nucala® group had significantly fewer exacerbations. Trial 3 assessed the effect of Nucala® on reducing the use of maintenance oral corticosteroids. Compared with placebo, the Nucala® group achieved greater reductions in daily maintenance oral corticosteroid dose, while maintaining asthma control. The change from baseline in the mean FEV1 was obtained in all 3 trials. Nucala® did not provide consistent improvements in the mean change from baseline in FEV1 when compared to placebo. There were no clinical trials conducted to assess the effect of renal or hepatic impairment on the pharmacokinetics of mepolizumab.

Recommendation: The recommendation is for Nucala® to be non-preferred.

Clinical Criteria:

- Quantity limit = 1 vial every 28 days.
- The patient must be 12 years of age or older AND
- The patient must have a diagnosis of severe persistent asthma with an eosinophilic phenotype as defined by pre-treatment blood eosinophil count of ≥150 cells per mcL within the previous 6 weeks or ≥ 300 cells per mcL within 12 months prior to initiation of therapy AND
- The patient has a history of 2 or more exacerbations in the previous year despite regular use of high dose inhaled corticosteroids (ICS) AND inadequate symptom control when given in combination with another controller medication (long-acting beta agonist [LABA] or leukotriene receptor antagonist [LTRA]) for a minimum of 3 consecutive months, with or without oral corticosteroids. Pharmacy claims will be evaluated to assess compliance with therapy. AND
- The patient has a pre-treatment FEV_1 <80% predicted AND
- The prescriber is an allergist, immunologist, or pulmonologist. AND
- The patient has a documented side effect, allergy, or treatment failure to Xolair.

For continuation of therapy after the initial 3 month authorization, the patient must continue to receive therapy with both an ICS and a controller medication (LABA or LTRA) AND have either a decreased frequency of exacerbations OR decreased use of maintenance oral corticosteroids OR reduction in the signs and symptoms of asthma OR an increase in predicted FEV_1 from baseline.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

c) Prestalia® tabs (perindopril arginine/amlodipine besylate)

- Prestalia® is a combination product containing the ACE-Inhibitor perindopril arginine and the CCB amlodipine besylate. Perindopril arginine is the L-arginine salt of perindopril, which is a pro-drug, hydrolyzed to perindoprilat. Amlodipine is a long-acting dihydropyridine calcium antagonist. It is indicated for the treatment of hypertension, to lower blood pressure (BP). It may be used in patients whose BP is not adequately controlled on monotherapy OR it may be

used as initial therapy in patients likely to need multiple drugs to achieve BP goals. The use of Prestalia® is not recommended in patients with heart failure. Prestalia® is a combination agent indicated to be used when monotherapy is not effective or for initial therapy when multiple medications are needed for adequate control. While it was found to be effective as compared with placebo and as compared with its individual ingredients, Prestalia® 10/14mg studied in one clinical trial did not provide any added benefit as compared with amlodipine 10mg monotherapy in black or diabetic patients.

Recommendation: The recommendation is for Prestalia® to be non-preferred.

Clinical Criteria:

- Remove ACE inhibitor/Calcium Channel Blocker combination criteria.
- Prestalia: The patient has had a documented side effect, allergy, or treatment failure to Amlodipine/Benazepril AND the patient is unable to take perindopril and amlodipine as the individual separate agents.
- Lotrel, Tarka: The patient has had a documented side effect, allergy, or treatment failure to the generic formulation.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

d) Tresiba® Insulin (degludec injection)

- Insulin degludec injection is a long-acting basal human insulin analog. It differs from human insulin in that the amino acid threonine in position B30 has been omitted and a side-chain consisting of glutamic acid and a C16 fatty acid has been attached. Insulin and its analogs lower blood glucose (BG) by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. It is indicated to improve glycemic control in adults with diabetes mellitus (DM). Tresiba® is not recommended for the treatment of diabetic ketoacidosis. Comes in dosage forms: 100U/ml or 200U/ml in a 3ml FlexTouch disposable prefilled pen. Numerous studies in various patient populations found Tresiba® to be non-inferior to insulin glargine long-acting for HbA1c reduction.

Recommendation: The recommendation is for Tresiba® to be non-preferred.

Clinical Criteria:

- TRESIBA FLEXTOUCH: Diagnosis of diabetes mellitus AND Prescription is initiated by an Endocrinologist AND The patient must have documented treatment failure with BOTH preferred agents.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation with amended clinical criteria to state: Prescription is initiated in consultation with an endocrinologist.

e) Varubi® Tabs (rolapitant)

- Rolapitant, the active ingredient of Varubi®, is a selective and competitive antagonist of human substance P/neurokinin 1 (NK1) receptors. Rolapitant is metabolized to form a major active metabolite, which has a mean half-life of 158 hours. It is indicated for use in combination with other antiemetic agents in adults for the prevention of delayed nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy. Varubi® should be given in combination with a 5HT3 receptor antagonist (RA) and dexamethasone according to administration tables published in the package insert. All regimens studied in the clinical trials included granisetron and dexamethasone, with the third drug in the regimen being either Varubi® or placebo. Administer Varubi® prior to the start of each chemotherapy cycle, but at no less than 2 week intervals.

Recommendation: The recommendation is for Varubi® to be non-preferred.

Clinical Criteria:

- Quantity limit 4/28days.
- Varubi: Medication will be prescribed by an oncology practitioner. AND patient requires prevention of nausea and vomiting associated with moderate to highly emetogenic cancer chemotherapy AND The requested quantity does not exceed 4 tablets per 28 days AND the patient has had a documented side effect, allergy, or treatment failure with Emend®.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

f) Vivlodex® Caps (meloxicam)

- Meloxicam, the active ingredient of Vivlodex®, is a nonsteroidal anti-inflammatory drug (NSAID). While the exact mechanism of action of NSAIDs, including Vivlodex®, is not known, it is thought that it involves inhibition of cyclooxygenase (COX-1 and COX-2). In vitro, meloxicam is a potent inhibitor of prostaglandin synthesis. It has analgesic, anti-inflammatory, and antipyretic properties. The indication is for the management of osteoarthritis pain. A multicenter, randomized, double-blind, placebo-controlled study was performed

to assess the safety and efficacy of Vivlodex® 5mg or 10 capsules as compared to placebo for the treatment of pain due to osteoarthritis of the knee or hip (N=402). The primary endpoint was the change from baseline to week 12 in the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) Pain Subscale Score. The mean baseline WOMAC Pain Subscale Score across treatment groups was 73mm using a 0 to 100mm visual analog scale (VAS). Results suggested that Vivlodex® 5mg (-36.52mm) and 10mg (-34.41mm) significantly reduced osteoarthritis pain as compared to placebo (-25.68mm), as measured by the changes in the WOMAC Pain Subscale Scores. As Vivlodex® has not shown equivalent systemic exposure to other formulations, it is not interchangeable with other Meloxicam formulations even if the total mg strength is the same.

Recommendation: The recommendation is for Vivlodex® to be non-preferred.

Clinical Criteria:

- Vivlodex: patient has had a documented side effect, allergy, or treatment failure to 4 or more preferred generic NSAIDs, including generic meloxicam.
- Removal of drugs from the NSAID PDL category which are no longer available or rebateable.
- Add Fenoprofen 400mg cap to non-preferred.
- Add Diclofenac 1% Gel to the Voltaren clinical criteria with additional: For approval of generic Diclofenac 1% gel, the patient must have had a documented intolerance to Brand Voltaren.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendation.

8. Therapeutic Drug Classes – Periodic Review: Jacquelyn Hedlund, MD GHS/Change Healthcare and Laurie Pedlar, RPH GHS/Change Healthcare

a) Antibotics, Vaginal

- No new drugs.
- No other significant changes.

Recommendation:

- No changes at this time.

Clinical Criteria:

- No changes at this time.

Public Comment: No public comment.

Board Decision: None needed at this time.

b) Bone Resorption Agents

- No new drugs.

Recommendation:

- Remove definition of treatment failure from each drug listed in the clinical criteria and replace with **, listing it once instead.
- Zometa Injection, Zoledronic Acid Injection (4mg): Diagnosis or indication is bone metastases from solid tumors, multiple myeloma, osteopenia or treatment of hypercalcemia of malignancy.

Public Comment: No public comment.

Board Decision: The Board unanimously approved the above recommendations.

c) Cytokine & CAM Antagonists

- Methotrexate was first used in 1951 for the treatment of rheumatoid arthritis and psoriasis. It is now available in oral, intramuscular, and subcutaneous routes of administration. Its use is highly effective for improving clinical outcomes of RA; however, if no response is seen with methotrexate use, it may be used in combination with other drugs, such as biologic disease-modifying antirheumatic drugs (DMARDs).
- Biologic response modifiers, including the cytokine and cell adhesion molecules (CAM) antagonists, are secreted by the immune system in response to an offending agent, and function to direct the immune response into the most effective pathway that will eventually result in elimination of the offender. In the past several decades, there has been an ever-growing interest that has led to the discovery of numerous cytokines and CAMs, which interact with the immune system in a variety of ways.
- New drugs since the category has been reviewed are Ixekizumab (Taltz®), rilonacept (Arcalyst®), tofacitinib (Xeljanz® XR).
- Medications in this class review can be used for a wide variety of diagnoses. Guidelines for their use and recommended dosing depend on the indication.

Recommendation:

Clinical Criteria:

Ankylosing Spondylitis: Injectables

- Cosentyx® (secukinumab) subcutaneous (Quantity limit = 8 pens or vials month one, then 4 pens or vials monthly) added as a non-preferred agent.

This is a new indication for the medication. It is already on the PDL in the Psoriasis: Injectable category.

- Combine Cimzia, Cosentyx, Remicade, and Simponi clinical criteria: patient has a diagnosis of ankylosing spondylitis (AS) and has already been stabilized on the medication being requested OR diagnosis is AS, and conventional NSAID treatment and DMARD therapy (e.g. methotrexate therapy) resulted in an adverse effect, allergic reaction, inadequate response, or treatment failure. If methotrexate is contraindicated, another DMARD should be tried. AND the prescriber must provide a clinically valid reason why both Humira and Enbrel cannot be used
- Additional criteria for Cosentyx and Simponi: Patient must be ≥ 18 years of age. Safety and efficacy has not been established in pediatric patients.

Gastrointestinal: Inflammatory Bowel

- Combine Entyvio and Simponi clinical criteria.

Psoriasis: Injectables

- No changes at this time.

Rheumatoid, Juvenile & Psoriatic Arthitis

- Remove Enbrel criteria, strike through Humira and change to "For all Drugs."
- Remove duplicated criteria from Actemra Subcutaneous, Actemra Intravenous Infusion, Cimzia, Remicade, Simponi Aria, Simponi subcutaneous, Kineret, Xeljanz, Orencia Intravenous Infusion, Orencia subcutaneous, and Stelara.

Interleukin (IL)-1 Receptor Blockers

- No changes at this time.

Miscellaneous

- No changes at this time.

Phosphodiesterase (PDE-4) Inhibitors

- No changes at this time.

Public Comment: Thomas Algozzine from Novartis highlighted attributes of Cosentyx and Gilenya.

Board Decision: The Board unanimously approved the above recommendations.

d) Growth Hormones

- No significant new studies or changes.
- Growth hormone deficiency (GHD) is a medical condition caused by problems with pituitary gland function. GH deficiency has a variety of negative health

effects including hypoglycemia in newborns, growth failure in later infancy and childhood, and poor bone density in adults.
- Mecasermin (Increlex®) is not to be a substitute for growth hormone treatment. It is indicated for use in children with severe primary insulin-like growth factor-1 (IGF-1) deficiency or with growth hormone (GH) gene deletion. Its use is not intended for secondary forms of IGF-1 deficiency, such as GH deficiency or malnutrition.

Recommendation:

Clinical Criteria:
- Remove Nutropin® from non-preferred side of the PDL as well as the clinical criteria.
- Add Zomacton® to non-preferred side of the PDL and add it to the clinical criteria with Genotropin, Humatrope, Nutropin AQ, Omnitrope, Saizen, Tev-Tropin.

Public Comment: No public comment

Board Decision: The Board unanimously approved the above recommendation.

e) Hereditary Angioedema
- New drug Ruconest®
- No significant new studies or changes.
- Hereditary angioedema (HAE) is a disorder characterized by spontaneous swelling of the submucosal and subcutaneous tissue typically involving the face, tongue, larynx, extremities, genitals or bowels. It results in significant morbidity and may have significant mortality associated with it as well if laryngeal swelling is present. There are multiple types of HAE sub-classified as type 1 (low C1-INH levels and low functionality), type 2 (normal C1-INH levels with impaired functionality), and previously labeled type 3 now termed HAE with normal C1-INH activity. These manifestations are a result of an autosomal dominant genetic mutation. Treatment approaches can be divided into treatment of acute attacks and long term prophylaxis. Acute treatment with plasma derived C1-INH has been available in Europe for over 30 years and has recently been approved in the US (Berinert®). In conjunction with its approval, additional medications targeting the bradykinin pathways (ecallantide and icatibant) have recently come to market as well as a recombinant version of C1-INH. The expansion of treatment options, as well as the ability of patients to provide self-administered treatments, has significantly improved the quality of life for patients with HAE types 1 and 2.

Recommendation: The recommendation is for Ruconest® to be non-preferred.

Clinical Criteria:

- Quantity Limit on Ruconest® 4 vial/fill.
- Ruconest: The diagnosis or indication is treatment of an acute Hereditary Angioedema (HAE) attack AND the patient has had a documented side effect, allergy, treatment failure or a contraindication to Berinert® or Cinryze®(Approval may be granted so that 2 doses may be kept on hand).

Public Comment: No public comment

Board Decision: The Board unanimously approved the above recommendation.

f) Multiple Sclerosis Agents

- No significant new studies or changes.
- New J-code drug alemtuzumab (Lemtrada®).
- Multiple sclerosis (MS) is a disease of the central nervous system (CNS) that was first diagnosed in 1849. It is considered a condition where the brain and other parts of the body are not able to appropriately communicate with each other. There is no known cure for MS. Therapies used to treat patients with multiple sclerosis (MS) are initiated for one of four purposes: (1) for the management of acute relapse, or periods of severe neurologic symptoms with corticosteroid therapy; (2) for the symptomatic management of chronic symptoms associated with neurologic damage such as paresthesias and hypesthesias, bladder and bowel dysfunction, or spasticity; (3) to improve walking, as demonstrated by an increase in walking speed; and (4) for the delay or prevention of future relapses and further neurologic damage. Most agents approved for the treatment of multiple sclerosis fall into the last categories. They are considered the mainstay of MS therapy, with the goal of modifying the disease course. All work by modulating the immune system to diminish the immune-based destruction of myelin sheaths in the central nervous system (CNS). Most disease-modifying therapies have minimal to modest effects, with bothersome side effects. The more efficacious agents are hindered by severe side effects, some of which are life-threatening.

Recommendation: No changes at this time.

Public Comment: No public comment

Board Decision: None needed at this time.

9. New Managed Therapeutic Drug Classes:

- None at this time.

10. Review of Newly-Developed/Revised Clinical Coverage Criteria and/or Preferred Products:

a) SSRI's

Clinical Criteria:

- Move all Fluoxetine tablets to non-preferred status.
- Move Escitalopram tablets to preferred status.
- Remove Luvox CR® from PDL as it no longer available.

Board Decision: The Board unanimously approved the above recommendation with amended clinical criteria to add Fluoxetine Sol to the preferred side of the PDL.

11. General Announcements: Mike Ouellette, RPh GHS/Change Healthcare

- Selected FDA Safety Alerts

FDA Drug Safety Communication: FDA revises warnings regarding use of the diabetes medicine metformin in certain patients with reduced kidney function
http://www.fda.gov/Drugs/DrugSafety/ucm493244.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

FDA Drug Safety Communication: FDA adds warnings about heart failure risk to labels of type 2 diabetes medicines containing saxagliptin and alogliptin
http://www.fda.gov/Drugs/DrugSafety/ucm486096.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

Opioid Pain Medicines: Drug Safety Communication - New Safety Warnings Added to Prescription Opioid Medications
http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm491715.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

FDA Alerts Healthcare Professionals About Clinical Trials with Zydelig (idelalisib) in Combination with other Cancer Medicines
http://www.fda.gov/Drugs/DrugSafety/ucm490618.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

12. Adjourn: Meeting adjourned at 8:12 p.m.